Needs Assessment for a Medical Monitoring Program for Former Workers, Rocky Flats Environmental Technology Site

July 1, 1997

University of Colorado Health Sciences Center
A. James Ruttenber, Ph.D., M.D., Principal Investigator
Michael J. Kosnett, M.D., M.P.H.
Tim Byers, M.D., M.P.H.
Ming Yin, M.S.
Janice Hartman, M.B.A.
David McClure, M.S.
Jason McCrea

National Jewish Medical and Research Center
Lee S. Newman, M.D., M.A., Co-Investigator
Elaine Daniloff, M.S.P.H.

New England Research Institutes
Anthony D. LaMontagne, Sc.D., M.A., M.Ed., Co-Investigator

Tri-County Health Department
John Martyny, Ph.D.

Acknowledgments

We acknowledge the Colorado Department of Public Health and Environment (CDPHE), Rocky Flats Worker Study, under the direction of Amy Warner, for developing the job exposure matrix that will be used to identify former workers who are eligible for medical monitoring. We also recognize Margaret Schonbeck of the CDPHE for providing consultation and liaison work with the current plant staff and former workers. Funding for the development of the job exposure matrix and the epidemiologic database was provided by the National Institute for Occupational Safety and Health.

Table of Contents

I. Introduction

In this report, we provide evidence for the need to establish a medical monitoring program for former workers at the Rocky Flats Environmental Technology Site (RFETS). We determined this need by first identifying the hazardous exposures that could result in chronic disease. We then developed eligibility criteria based on those used in other medical monitoring programs and on criteria that have been used by researchers and regulatory agencies to justify medical surveillance. We then estimated the number of former workers who would be eligible based on these criteria.

To make these assessments and recommendations, we used many data sets that have been created for the epidemiology studies of RFETS workers that are being conducted by the University of Colorado Health Sciences Center (UCHSC) and the Colorado Department of Public Health and Environment (CDPHE). These studies include: 1) the creation of a database that records internal and external radiation exposures and doses for individual workers; 2) the construction of a job exposure matrix (JEM) for the entire plant site to estimate exposures to chemicals that are carcinogens or that produce other chronic health effects, 3) a cohort study of cancer incidence and mortality for all production-era workers, and 4) nested case-control studies of selected cancers that involve detailed calculations of internal radiation doses. The plans for this work are documented in both the protocol for this DOE project, and in the protocol for the epidemiology studies funded by the National Institute for Occupational Safety and Health (NIOSH). Both are available upon request.

Finally, for the specific exposures of interest, we described the health impacts that would be anticipated based on a review of the scientific literature. We also described the screening tests that could be used to detect these health effects and identified the ones we would recommend for a medical monitoring program.

II. Identifying the Population of Former Workers Eligible for Medical Monitoring

Although the best available scientific information should be used in determining who is eligible for medical monitoring, this alone is not sufficient. In addition to being scientifically based, eligibility criteria must also be acceptable to the workers being screened; otherwise, participation in the program may be adversely affected. Accordingly, our final eligibility criteria will be determined in consultation with the Rocky Flats Former Workers' Advisory Group (FWAG). This group was organized in December 1996, and continues to meet on a regular basis (four meetings thus far, plus numerous individual contacts with the 16 members of the group). In Phase I of our project, we have found that (1) determination of eligibility criteria is a major concern of the FWAG, and (2) communication of the essence of the conceptual and scientific basis of the alternatives will take time, and is an essential precondition to informed discussion with the FWAG. We therefore believe that it is premature to define eligibility criteria at the present time, but plan to do this during the first year of Phase II.

Even though it is best to determine final eligibility criteria at a later date, we think that there is enough data to determine whether or not medical monitoring should be conducted at RFETS. In this report we will demonstrate that there is a scientifically justifiable need for establishing a medical monitoring program and that we have the

ability to identify eligible former workers and specify appropriate screening procedures. To accomplish this goal, we will develop preliminary, scientifically-based criteria for determining eligibility and then determine the number of workers who meet these criteria.

From our databases developed for the epidemiology studies, we have identified 19,218 persons who were former workers at the RFETS and who are not known to be dead. Of these, the vital status is uncertain for 4,058 (21%). We will soon submit a list of these workers to the National Death Index to identify those who have died between 1979 and 1995. Of the entire group, 14,430 were employed between January 1, 1951 and December 30, 1989--the period of weapons production at RFETS. The remainder were employed in cleanup activities after this period. The category "production workers" includes both employees of prime contractors and employees of sub-contractors or consultants. We have some data on employment classification, and will probably be able to identify employees of prime contractors and sub-contractors in the future, if necessary. For the group of all former workers, we have Social Security numbers for everyone, and last known addresses for 18,821 (98%). Since data for exposures during cleanup operations are not readily available, we have focused our efforts on former production workers. Table 1 summarizes descriptive data for this group.

Determining eligibility for inclusion in a program of medical monitoring is difficult for a number of reasons: 1) there are few written guidelines for establishing selection criteria, 2) Although a risk-based approach is most supportable by scientific criteria, adequate data for making quantitative risk estimates may not be available, and 3) the lack of similar data at each site will make it difficult to apply quantitative criteria uniformly across all Department of Energy (DOE) facilities.

The determination of eligibility criteria is further complicated by the fact that there are already two medical surveillance programs in place--the Beryllium Health Surveillance Program (BHSP) and the Medical Monitoring of Former Radiation Workers Program (MMFRWP), which are described below. Since both programs have already established eligibility criteria and protocols for screening tests, there are existing precedents and expectations in the RFETS former worker population.

In describing the population of eligible workers and discussing eligibility criteria, we have considered each exposure separately. Clearly, a worker who has a high dose from external penetrating radiation is likely (but not certain) to have a high internal deposition from Pu or Am. If such a worker was deemed eligible by both criteria, he or she would receive the same set of medical monitoring tests. We therefore emphasize that summing the number of eligible workers for each exposure will overestimate the total number of workers who are eligible for medical monitoring. Although we could account for this overlap, we chose not to do so because the eligibility criteria are still subject to further discussion. Once final criteria have been established, we will account for the overlap and make more accurate estimates of the total number of workers eligible for screening due to one or more hazardous exposures.

A. Eligibility Based on Exposures to Ionizing Radiation

1. Examples of Medical Monitoring Programs for Persons

Exposed to Ionizing Radiation

There are only a few examples of medical monitoring programs that have been instituted for radiation workers and others exposed to ionizing radiation. These are described below.

Rocky Flats Medical Monitoring of
Former Radiation Workers Program

The Medical Monitoring of Former Radiation Workers Program (MMFRWP) is a voluntary program for the health monitoring of former workers that began in 1980. The program is managed by the Health Effects Department (HED) which is part of DynCorp of Colorado, one of the first-tier contractors to Kaiser-Hill, the current prime contractor at RFETS. It provides physical examinations and dosimetric measurements every three years for workers who have received the highest external and internal exposures to ionizing radiation. The eligibility criteria are based on examining 200 to 250 workers per year. To date, approximately 400 workers have been enrolled, based on any one of the following criteria:

a) Detectable lung deposition of Pu 239/240 or Am 241;
b) 10% or more of the maximum permissible systemic burden for Pu 239/240 or Am 241 (approximately 8 nCi) or 20% or more of the maximum permissible lung burden of Pu 239/240 or Am 241 (approximately 3 nCi), based on analyses of urine assays;
c) An annual effective dose at termination of 500 mrem or more, based on internal dosimetry models;
d) A wound with measurable Pu or Am deposition
e) Lifetime external equivalent dose of 20 rem or more
f) Evidence from review of records or a self-reported exposure suggesting the likelihood of a substantial internal deposition with no data adequate to characterize the deposition.

Eligible workers have been identified through a review of separate computer dosimetry files and hard-copy records. To date, there is no comprehensive database that identifies all former workers and records doses and internal depositions; therefore, the extent to which all eligible workers have been identified is not clear. The databases we have developed for the epidemiologic studies will improve the ability to assess eligibility for all workers.

Fernald

The medical program specified in the class-action settlement agreement in a lawsuit against the Fernald Feed Materials Production Center (FMPC) (United States District Court Southern District of Ohio, Western Division, 1994) is perhaps the example of eligibility criteria that are of relevance to Rocky Flats workers. Eligible workers include all persons who were employed for six consecutive work weeks and all persons

who were employed by a contractor and who were present at the FMPC for at least six consecutive work weeks and who were no longer present after December 31, 1981. These eligible workers are entitled to receive an initial physical examination and annual follow-up examinations. Dose distributions have been estimated for FMPC workers (Franke & Gurney, undated), and about half the workforce received annual doses to the lung less than 15 rem for most of the production years.

Another settlement of a class-action lawsuit has established a medical monitoring program for persons who live near the Fernald facility. The eligibility requirement is residence within a five-mile radius of the plant. Although dose estimates have been made for this group through a comprehensive dose reconstruction project, these data became available after the settlement, and were not used to establish eligibility.

Hanford

Another source of guidance for establishing eligibility criteria is the Agency for Toxic Substances and Disease Registry (ATSDR) draft final document, Consideration of Medical Monitoring for Hanford (ATSDR, 1996a). This document specifies recommended criteria for members of the general public exposed to iodine-131 from the Hanford nuclear facility between 1946 and 1951. The criteria are: 1) an estimated equivalent dose of 10 cGy (rad) to the thyroid, or 2) a person who was between 0 and 19 years of age between 1946 and 1951 and who resided in a high exposure area for a minimum of 30 days for 1945, or 90 days for the period 1946-1951.

Oregon State Penitentiary

In the late 1980s, the Oregon Legislative Assembly passed a bill mandating that the Oregon Department of Corrections offer annual medical evaluations to prisoners who were subjects in experiments that involved the administration of X-radiation to the testicles between 1963 and 1973. During this period, 67 male prisoners received doses to the testicles that ranged between 8 and 600 rad.

Summary of Existing Criteria

In summary, the eligibility criteria for medical monitoring have not been consistent between groups exposed to ionizing radiation. Furthermore, most of the criteria have not been based on estimates of cancer risk. It appears that any criteria for eligibility will be somewhat arbitrary, and therefore controversial. It is desirable that the final criteria, to the greatest extent possible, be similar for the different sites within the DOE complex, and have concurrence from representatives of former workers at all sites.

2. Eligibility Criteria for External Exposures to Gamma Rays and Neutrons

Identification of Exposed Former Workers

From the data compiled for the cancer epidemiology studies, we have created a database that lists the lifetime cumulative whole body doses from gamma rays and neutrons for most former workers at RFETS. This database lists annual doses for the

years after 1976, and a cumulative dose for the years up to and including 1976. These data are summarized in Table 2, and indicate that cumulative penetrating doses are available for 12,822 (67%) of 19,218 former workers. Of this group, 9,105 (71%) were production workers, and 3,717 (29%) worked in cleanup. It is not yet clear why external dosimetry data are available for so few former workers.

Health physicists at RFETS have acknowledged that external doses from neutrons have been inaccurately estimated for the years between 1952 and 1971. The HED has established a program to identify current and former workers who were exposed to neutrons and recompute doses for them by retrieving personal dosimeters that have been kept in storage. It is anticipated that it will take a number of years to make these dose estimates for all former workers. It is therefore unlikely that they can be used in establishing eligibility criteria within DOE's stated time frame.

In order to include the contribution from neutron exposure in the estimates of cumulative external whole-body doses, we will have to make less accurate estimates based on combinations of specific job classifications and calendar years for buildings that housed production processes that exposed workers to neutrons. Notional (or estimated) doses assigned in this manner will be based on worst-case scenarios.

For former workers with no record of cumulative radiation dose, we will attempt to reconstruct their work histories using the JEM and then estimate doses using dose distributions for workers with the same or similar job classifications. For workers with no JEM data, we could reconstruct work histories and job classifications through questionnaires and interviews.

Determination of Eligibility

The MMFRWP has an eligibility criterion of a lifetime external whole body equivalent dose of 20 rem or greater. Until the data from this program can be reviewed thoroughly and a decision made on eligibility criteria for the entire DOE complex, we suggest using the MMFRWP eligibility criteria. For former workers who were assigned notional doses based on job and organization codes in the JEM, the criteria for eligibility would probably be lower to account for uncertainties in the estimated dose. Based on the data in Table 2, 199 (2%) of former workers with external dose data would be eligible if a total penetrating dose of 20 rem or larger were used as the eligibility criterion.

3. Eligibility Based on Internal Exposures to Isotopes of Pu & Am

Identification of Exposed Former Workers

There are no computerized records of doses from internal exposures to isotopes of Pu and Am that cover all production years at RFETS. The most detailed data for internal dosimetry are the hard-copy dosimetry files for each worker, which are stored in the Denver Federal Records Center. The MMFRWP has attempted to identify the former workers with the highest internal doses, using a variety of records. Their roster is the most reliable one for workers who received high cumulative internal doses. For this group, detailed organ doses have been computed using the Computerized Internal

Dosimetry (CINDY) program developed by the Battelle-Pacific Northwest Laboratory. Although detailed doses have not been estimated for many other former workers, they are now being computed for current workers.

The Radiation Protection Division at RFETS prepared a database that summarized the systemic deposition of isotopes of Pu and Am for all current and former workers during the period of weapons production at RFETS. For workers still employed between 1989 and 1991, estimates were made during this period (99% were made before the end of 1989); for those who left employment before this period, estimates were made for the year of termination. This database records systemic burden as the percent of maximum permissible deposition, which is 0.04 uCi for isotopes of Pu and 0.05 uCi for all isotopes of Am. These maximum depositions are based on the deposition in bone that would yield a 50-year committed dose to the bone surface of about 50 rem.

Although a hard-copy report of the results of these analyses was produced, the computer files with raw data, analysis programs, and results were all destroyed. For the cancer epidemiology study being conducted by CDPHE and UCHSC, these data are being entered into a computer database so that they can be used to assign quantitative estimates of internal exposure for the production-worker cohort. To date, data have been entered for 8,831 former employees of prime contractors (Table 3); data for sub-contractors are still being entered into a computer database. We plan to use data for both groups in the final determination of eligibility.

From the Radiation Protection Division, we have obtained a data set of lung count data for all workers. Lung counting was not a routine procedure until the early 1970s, and it is not clear how frequently workers were counted. We understand, however, that at some point it became standard procedure to perform a lung count when a worker terminated employment. Lung counts were performed for Pu-239, Am-241, U-238, and Th-234 (Table 4); as indicated, 492 (2.6% of all

former workers who were counted) had a positive lung count for at least one of the radionuclides. We have not yet determined production status for this group.

Determination of Eligibility

The MMFRWP uses the eligibility criteria that were described above. Until the data from this program can be reviewed thoroughly and a DOE complex-wide decision made on eligibility criteria, we propose using these MMFRWP eligibility criteria. The data that have been collected by the MMFRWP are the most accurate from a dosimetry standpoint; it is not clear, however, whether the criteria have been applied to all former workers. We plan to obtain the dosimetry data from the MMFRWP and determine the best way to identify all eligible former workers. Based on the data we have obtained from the Radiation Protection Division, 296 (3.3% of former production workers who were analyzed) would be eligible by virtue of having 10% or more systemic burden of Pu-239/241; 30 (0.3% of former production workers who were analyzed) for Am-239/241, and 492 (2.6% of all former workers who were counted) for a positive lung count. We are not aware of databases that record wound counts for former workers.

4. Eligibility Based on Combined Internal and External Exposures to Ionizing Radiation

Identification of Exposed Former Workers

There is no satisfactory method for combining dose estimates from external penetrating radiation with estimates of systemic burden. The currently recommended methodology for assessing the combined risk from internal and external doses involves computing an effective dose by scaling organ doses from internal exposures based on their risk for fatal cancer and other health effects. Because we will not have organ doses from internal exposures for the entire former worker cohort, we will not be able to compute effective doses. Instead, we will have to apply an alternative method. The simplest method would be to establish the final separate eligibility criteria for external doses and systemic burdens and then, for each worker, divide the systemic burden and cumulative external penetrating doses by their respective criteria levels and add the results. Workers with totals of one or more would be eligible. This method is similar to the one used for determining whether exposures to combinations of radionuclides or other pollutants exceed regulatory guidelines.

5. Screening for Disease in Radiation-Exposed Workers

Although isotopes of Pu and Am concentrate in a few organs (lung, liver, and bone), gamma and neutron radiation yield similar doses to all organs. Moreover, current data and theories suggest that persons exposed to ionizing radiation are at increased risk for all types of cancer. Recommended cancer screening tests are described in Section III.A.

There is recent evidence from both Russia and the United States that workers with Pu in their lungs may be at risk for pulmonary fibrosis. Dr. Lee Newman is the principal investigator on a NIOSH grant to study this possible exposure-disease relationship. We will use the results of his research to guide us in assessing the appropriate medical monitoring procedures for this group of workers. Since workers with lung burdens of Pu will be eligible for cancer screening, they will already be identified and additional screening tests will be easy to implement.

B. Eligibility Based on Exposures to Beryllium

Identification of Exposed Former Workers

There are no records at RFETS that systematically identify all workers who could have been exposed to Be. The JEM could be used to identify workers who are at risk for disease by virtue of their job title, work location, and years of employment. Based on initial assessments, there are 972 former whorkers who had a high risk for exposure to Be (Tables 8 & 9). Because persons can become sensitized to Be after only brief exposures to small concentrations, and because workers with most any job description could have come in contact with Be during weapons production, this approach may not identify all workers who have been placed at risk. For these reasons, the BHSP (the

current surveillance program for RFETS workers managed by the HED) has offered screening for sensitization to Be to all current and former workers.

Determination of Eligibility

The BHSP has offered a program of Be screening to all current and former RFETS workers regardless of their exposure status. It is not clear, however, to what extent workers with the highest exposures have been screened. In Phase II, we will compare the listing of persons who have been screened in the BHSP with the workers identified as at high risk through the JEM.

The goal of the review of beryllium exposures will be the construction of a single cohort of workers who had the potential for exposure to beryllium, based on data from the JEM, or based on self reports of beryllium exposure collected by the BHSP, or by a questionnaire to be administered in the notification process of the medical monitoring program.

The definition of a potentially beryllium-exposed individual will be broad; it will include former workers who were security guards, construction trades workers, secretaries, and office staff. We plan to use the JEM to identify this group. As described below, this group will be subdivided into high and low exposure groups. The broad-based eligibility criteria is based on published data (Newman 1989; Kreiss 1989; Kreiss 1993a, 1993b; Kreiss 1996) demonstrating that while there are job-related and exposure-related elevated risks for chronic beryllium disease (CBD), individuals with low-level exposure can be affected. As such, we propose two tiers of surveillance based on risk category.

Risk Stratification

The high risk group, which will be eligible for more frequent surveillance (see below), will be defined in four ways, two of which are based on the frequency of disease among workers who have held particular job titles at the Rocky Flats Plant, a third based on the JEM, and a fourth on previous beryllium surveillance test results from the BHSP.

First, we will rely on published data from our previous study (Kreiss 1993a), in which we observed that there were at least three high risk job titles at the plant: 1) machinist, 2) metallurgical operator ("met op"), and 3) chemical control operator ("chem op"). Secondly, we will review the data from the current BHSP and calculate CBD and beryllium sensitization frequencies by job title, in a manner similar to what we previously published, to determine if there are additional high risk jobs warranting greater surveillance. Third, we will identify workers with high potential for exposure as illustrated in Tables 8 and 9. Fourth, there is a subset of individuals who have already undergone testing in the BHSP but who have been found to have either a single abnormal beryllium lymphocyte proliferation test (BeLPT) (no confirmed second abnormal result) or who have a single abnormal B-reading of a chest radiograph (but no confirmed second B-reading of 1/0 or greater). These individuals would be included in the high risk subgroup, even if their job title qualifies them for the low risk group.

The low risk group will consist of all other individuals who meet the general eligibility criteria as determined by the JEM and self reports and did not meet criteria for high risk surveillance.

C. Eligibility Based on Exposures to Other Chemicals

1. Determining Exposures with a Job Exposure Matrix

For the cancer epidemiology study, potential chemicals of concern with respect to cancer or other chronic diseases were evaluated by reviewing inventories of chemicals used throughout the production history at RFETS. These inventories were reported in the ChemRisk (1991a,b; 1992) evaluations for off-site chemical releases generated for the dose reconstruction project for Rocky Flats offsite exposures conducted by the CDPHE. The list of chemicals from this review was then used as the basis for conducting detailed interviews with current and former workers who had knowledge of work practices and job-related exposures for the production period at RFETS. We first converted about 7,500 job titles into 140 general job categories and 200 organizational units into 70 genaral organizations, based on similarity of activity and exposure. We then made quantitative estimates of annual intakes (both low, average, and high, along with the type of frequency distribution) for every combination of general organization and job in each building for each production year. Since industrial hygiene data were not available for most exposures, we based these estimates on published data for similar processes in other industries in addition to available industrial hygiene data for RFETS. The chemicals for which estimates were made are listed in Table 5.

We are now in the process of combining the intake estimates for the organization/job/building/year combinations with a database that specifies such combinations for each individual worker. This database was produced by entering data from hard-copy strength report data for one month of each year for the entire production period. The strength reports were used by the personnel department to keep track of the number of workers employed in different organizations and buildings throughout the Rocky Flats complex. The job exposure matrix (JEM) will finally be created by linking the two databases.

<u>Identification of Exposed Former Workers</u>

The JEM is not yet complete. Although we have assigned general organization and job codes to all workers, annual quantitative estimates of intake have not been made for all general organizations and jobs. For this needs assessment report, we first identified the annual intake that would trigger medical monitoring for each chemical (as discussed below), and then had our industrial hygienist, Dr. John Martyny, identify the combinations of general organization, general job, building number, and year of production that would result in intakes at or above this intake criterion. We then searched the preliminary JEM database and counted the number of individual workers who met these criteria.

Based on initial analyses, it appears that there are data in the JEM for over 80% of former workers. For those workers not listed, we will have to determine exposures by

other methods, such as questionnaires administered by mail or phone or by assigning notional intakes based on data for other workers with similar combinations of general organization and job, building number, and year of employment.

Determination of Eligibility Based on OSHA Criteria and Precedents

For each chemical in Table 5, we reviewed industrial hygiene, toxicology, and epidemiologic data to identify measures of exposure intensity and duration that could be associated with chronic toxicity. Risk-based eligibility for medical surveillance can be based on measures of excessive exposure or on the occurrence of sentinel health events in a given worker population (NIOSH, 1988). Measures of excessive exposure may be qualitative (e.g. the occurrence of accidental/emergency exposures) or quantitative (e.g. exposure levels correlated with specific levels of risk using risk assessments based on previous epidemiologic or animal studies).

There are existing precedents for eligibility criteria, most notably the legal requirements contained in Occupational Safety and Health Administration (OSHA) standards. While OSHA standards may not be legally binding for former DOE worker exposures, they do represent some of the best articulated and justified occupational screening rationales currently available. For 4 of the 11 chemicals (asbestos, formaldehyde, lead, and methylene chloride) in Table 5, there are full OSHA 6(b) standards with medical surveillance requirements (Table 6). Exposures to each of these 4 chemicals can lead to long-term and serious health effects, such as cancer, lung disease, asthma, and neurobehavioral dysfunction. The medical surveillance requirements of the OSHA standards for these chemicals were designed in part to address these long-term cancer and non-cancer health risks. The medical surveillance eligibility criteria or triggers for each chemical are listed in Table 6. These were then used to calculate cumulative yearly exposure triggers for former workers in (exposure unit)-hours per year, allowing for direct comparison to exposure estimates generated in the JEM (right-most column, Table 6).

For 7 of the 11 chemicals to which Rocky Flats workers were exposed, there are Permissible Exposure Limits (PELs) in OSHA's Z-Tables, but medical surveillance requirements are not currently in place (Table 7). For these 7 chemicals, we have identified one eligibility criterion that is most common to all OSHA medical surveillance standards: exposure at or above the action level (usually 50% of the PEL) for 30 or more working days per year. To best represent a conservative occupational exposure limit (OEL) for each chemical that is based on all available evidence, we have also identified American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs) and NIOSH Recommended Exposure Limits (RELs) and applied a 50% action level factor to the lowest numerical OEL.

This latter approach is based on the following rationale: (1) OSHA standards and the other OELs are health risk-based, (2) each of the 7 exposures can lead to long-term and serious health effects, such as cancer, liver disease, and chronic beryllium disease, and (3) this eligibility criterion was considered in OSHA's Advance Notice of Proposed Rulemaking for a Generic Medical Surveillance Standard (OSHA, 1988).

These OSHA precedent-based eligibility criteria for cancer and other chronic

diseases (Table 6 & 7) were used to identify eligible workers, as described above. The estimated number of eligible workers for average and high exposure conditions are listed in Table 8. The total number of workers eligible for medical monitoring would likely be much fewer than the sum of the workers identified for each chemical, as many workers were exposed to more than one chemical, and the same screening tests may be recommended for different chemicals.

Determination of Eligibility Based on LOAELs

Another quantitative risk-based approach can be performed using the human Lowest Observed Adverse Effect Levels (LOAELs) found in the scientific literature. From the literature tabulated in Appendix A, we selected the LOAEL for the most sensitive non-cancer health effect for each chemical and estimated the yearly cumulative exposure that would correspond to the LOAEL (second column of Table 8). As described above, these annual intakes were then compared with average and high JEM exposure estimates to estimate the number of workers that would be eligible for medical surveillance using these criteria.

Alternate Eligibility Criteria

Alternate eligibility criteria include the number of years in a job or jobs with any exposure to a given agent or group of agents (e.g. chlorinated solvents). This approach would be very similar to those described above, because the specific jobs and the number of years worked could be derived from the JEM in a manner similar to the one described above. The advantages of this approach are that it would be simpler to communicate to former workers, it would reduce the reliance on uncertain quantitative estimates of annual intake, and it would be more consistent with strategies that may be used at the DOE sites for which JEMs have not been constructed.

The occurrence of sentinel health events or effects can also be used to trigger medical surveillance for specific groups of workers as described for beryllium workers in Section II.B. However, the identification of sentinel health events is of limited effectiveness unless the health effect of interest is pathognomonic for a specific exposure (such as beryllosis and asbestosis). Although cases of CBD and asbestosis have been identified in the former worker population at RFETS, the JEM-based approach is probably more comprehensive and conservative.

D. Exposures to Other Agents

We think we have identified and estimated almost all possible exposures to RFETS former workers. We have not, however, evaluated exposures to electromagnetic fields (EMFs) and noise. Since there is still controversy over whether EMFs increase the risk for cancer and because we have limited data on EMF exposures for former workers, we have not assessed risk and screening approaches at this time. To date, we have no data on noise levels that occurred during the production era. If we can use the JEM to identify workers at risk, then it may be appropriate to offer routine audiometry to screen for noise-induced hearing loss in the former worker population.

Because the JEM was designed primarily to detect exposure to chemical carcinogens for groups of workers in epidemiologic studies of cancer, we did not identify

agents or make exposure estimates for rare exposures that only affected small groups of workers, or for exposures that could not be linked to specific combinations of general organizations and jobs. It is likely, therefore, that the JEM has missed some agents that placed a comparatively small number of workers at risk for disease. We may be able to identify such exposures during the notification phase of medical monitoring, when workers will be asked to review our data on their work histories and exposures, and to identify other jobs and exposures that we have overlooked.

III. Anticipated Health Impacts for Specific Exposures

In the following sections we identify the anticipated health impacts from the exposures described in Section II. We also describe and discuss screening tests that might be used to detect these health effects and benefit the health of former workers. The data supporting the assessments of health impacts from chemical exposure are included in Appendix A.

A. Cancer (Ionizing Radiation)

We have reviewed the protocols for three medical monitoring programs (the Rocky Flats MMFRWP, Fernald area residents, and former and current prisoners in the Oregon State Penitentiary) that have been designed to assess cancer and other diseases for groups of persons exposed to ionizing radiation. We also know that there are other programs for which we have no documentation at this time (Fernald workers, for instance). Table 10 summarizes the components of each protocol. The primary health risk of interest for each of the three groups is cancer, but the Rocky Flats and Fernald programs also offer tests for other diseases, as well as tests that are not generally recommended for cancer screening--even for high risk groups. The protocol recommended for the Oregon State prisoners illustrates a more targeted approach, with diagnostic procedures that focus on the organ of interest.

Current data and theories suggest that persons exposed to ionizing radiation are at increased risk for all types of cancer. The degree of increased risk depends on radiation dose, the magnitude of exposure to chemical carcinogens in the workplace, and non-occupational factors, such as tobacco, diet, and hereditary factors. Because of the occupational exposure to carcinogens, we recommend evaluating eligible workers for all cancers for which there are reliable screening tests that are recommended for the general population. Based on recommendations from the U.S. Preventive Task Force (1966) and other reports (Byers et al., 1997a, b), we recommend the following:

1. A complete medical history and review of systems to determine the need to refer the subject for additional tests intended to diagnose cancer or other diseases at an early stage;

2. A routine physical examination for diagnosis of cancer and other diseases and for determining the need for additional diagnostic tests; special attention will be paid to signs of respiratory disease, with referral for additional testing when

appropriate;

3. Test for fecal occult blood and flexible sigmoidoscopy for persons age 50 or older;

4. Careful palpation of the thyroid gland by a trained physician and a survey of signs and symptoms of thyroid disease with additional diagnostic tests if indicated;

5. Breast examination and screening mammogram for women age 40 or older;

6. Digital examination of prostate for men age 50 and older, and the offering of a blood test for prostate-specific antigen;

7. An appraisal of cancer risks from occupational and environmental exposures and lifestyle factors and counseling to develop a personal plan for screening and risk reduction;

8. An appraisal of each worker's access to routine diagnostic services through health insurance, managed care plans, or other sources and development of a plan to obtain such services at the recommended age-based frequency;

The medical history, routine physical exam, cancer screening tests, and counseling would be offered only once to all eligible workers. For persons without access to routine diagnostic services, a routine physical examination will be offered every three years. A review of systems and history of recent changes in signs and symptoms of disease will be offered annually along with diagnostic tests for cancer of the thyroid, breast, colon and rectum (fecal occult blood test), and prostate annually. Sigmoidoscopy would be offered every 5 years.

B. Beryllium Disease (Beryllium)

Based on both the published literature and the past experience of the BHSP, we propose a modification of the existing BHSP testing protocol. This modification still relies on the blood BeLPT and on the chest radiograph, but at different intervals than currently offered. It also would call for a modification of the clinical evaluation portion of the protocol, in order to be less invasive and less costly.

The cornerstone test of the program will be the blood BeLPT. We propose, however, that testing be done in all individuals (high and low risk groups) as a one- time baseline, and that high risk individuals receive subsequent blood testing every two years; low risk individuals would be tested every four years. Single abnormal tests will be confirmed with a second blood BeLPT prior to referral for clinical evaluation.

Chest radiographs have proven to be relatively insensitive and to have very low positive predictive value for CBD when compared with the blood BeLPT (Kreiss 1993b;

Newman 1989; Newman 1994; Kreiss 1996). In the BHSP experience to date, of 64 persons diagnosed with CBD, 5 had abnormal chest X-rays but normal blood BeLPTs. Thus, we propose decreasing the frequency of x-ray testing of the workforce. Both high and low risk groups would receive a baseline chest radiograph and have x-rays repeated every four years (unless a subject happened to be in the asbestos surveillence group as well).

Clinical examination and symptom reporting have been shown to have low yield in the detection of CBD, proving both insensitive and non-specific. As such, we are not recommending clinical examination as part of the surveillance program. Workers in the high risk group who have symptoms compatible with CBD, e.g., shortness of breath, persistent dry cough, unexplained fatigue, night sweats, may be referred for clinical evaluation in this program at the discretion of the program director.

One limitation of the blood BeLPT has been the rate of uninterpretable or equivocal test results (approximately 6%). These tests have, in the past, led to repeat venipuncture and blood BeLPTs. Some individuals continue to have equivocal test results, leading to sometimes six or seven blood tests, incurring both expense and undermining former worker confidence in the testing program. Recently published data support the use of the beryllium sulfate patch test to resolve these equivocal cases in former workers no longer exposed to beryllium (Bobka, JOEM in press). The patch test is the *in vivo* demonstration of beryllium-specific sensitization (an *in vivo* BeLPT). It can be performed safely and at a cost which is comparable to approximately two blood BeLPTs. We propose that participants who have two equivocal/uninterpretable blood tests be patch tested. Similarly, individuals who have had a single abnormal blood BeLPT not confirmed in a second test (or in which the second test is equivocal or uninterpretable) be referred for patch testing. A negative patch test would place an individual back in routine surveillance as a non-sensitized individual. A positive patch test to beryllium sulfate would define that individual as beryllium sensitized and make them eligible for clinical evaluation.

C. Cancer (Chemical Carcinogens)

Except for lead, all chemical agents described in Section II and Table 5 are considered to be potential human carcinogens. Although there is evidence that these carcinogens have some specificity with regard to target organs (asbestos, for instance), most have not been studied extensively enough to rule out the ability to cause cancer at a number of sites. We therefore recommend that former workers determined to be eligible by the criteria proposed for one or more chemical carcinogens (including asbestos) be offered the same medical monitoring protocol as recommended for cancer screening in persons exposed to ionizing radiation. In cases where there is an unlikely exposure-disease relation (asbestos and breast or prostate cancer, for instance), it may be reasonable not to offer screening. The implementation of a targeted approach must be considered along with its acceptability to workers and viewed in light of the screening tests recommended for the unexposed general public.

D. Asbestosis (Asbestos)

A risk of asbestosis exists for former workers whose cumulative asbestos exposure is approximately 10 fiber-yr/cc (and possibly lower if exposure was primarily to amphibole asbestos) (Appendix A). Although the benefits of secondary prevention are limited, surveillance with a combined battery of respiratory questionnaire, history and physical exam, chest x-ray, and spirometry represents a reasonable approach, and is mandated by OSHA. Because of the long latency possible in asbestosis (20 to 40 years), repeat surveillance every 2 years may be indicated, beginning 15 years after the first identifiable exposure.

E. Liver Disease and Neurobehavioral Effects (Carbon Tetrachloride and Chlorinated Solvents)

Exposure to carbon tetrachloride and the chlorinated solvents--particularly perchloroethylene--has been associated with hepatotoxic and adverse neurobehavioral effects at levels of exposure in the range of 10 to 20 ppm and higher (Appendix A). The persistence of these effects in workers removed from exposure has not been well studied, but some evidence suggests improvement may occur if the insult was not severe. Medical surveillance for hepatic damage or insufficiency may be accomplished by measurement of serum bilirubin and serum transaminases. Recent data suggest that hepatic ultrasound may be a more sensitive indicator of early chronic hepatotoxicity, but the lack of extensive validation, and the attendant infrastructural requirements of the technique, diminish its utility in large scale screening. Surveillance for chronic, persistent neurobehavioral effects may be accomplished with use of a structured questionnaire; however, positive findings on this nonspecific instrument will require referral outside the context of the surveillance program for a detailed evaluation. Surveillance for these non-cancer endpoints can be terminated for workers whose initial evaluation is negative. Those with positive findings should undergo follow-up surveillance on an annual basis.

F. Respiratory, Dermal, and Renal Effects (Chromium)

Low level exposure to chromic acid aerosol, in the range of 0.001 to 0.002 mg/m^3, has been associated with inflammation or atrophy of the nasal mucosa (Appendix A). Slightly higher levels, in the range of 0.002 - 0.020 mg/m^3 have been associated with transient obstructive patterns on spirometry; and sensitization to chromates is a relatively rare cause of occupational asthma. Dermal or aerosol contact with chromium, even at low levels, is a well established cause of allergic contact dermatitis that may be particularly persistent. Airborne exposure to chromium has been associated with an increase in low molecular weight proteinuria in some studies, but evidence for chromium's role as a consistent cause of clinically significant nephrotoxicity is lacking.

In medical surveillance of former workers with prior exposure to chromium, evidence of nasal inflammation or atrophy can be readily determined on physical exam. Surveillance for asthma can be accomplished through a respiratory questionnaire, physical examination, and spirometry performed with and without bronchodilator. If

spirometry is negative in the face of a positive history, methacholine challenge testing may improve the sensitivity of the surveillance regimen, but its utility in a surveillance program is hindered by its high cost. Surveillance for symptomatic contact dermatitis, possibly due to chromium, can be easily accomplished through a history and physical examination. Recommendations may be then be offered for specific dermatologic testing, and secondary prevention may be accomplished through avoidance of further exposure, and pharmacologic therapy.

Laboratory surveillance for a chromium associated decrement in renal function can be accomplished by measurement of serum creatinine. Although measurement of urinary retinol binding protein may serve as an earlier biomarker of nephrotoxicity, the lack of evidence demonstrating that chromium nephrotoxicity may first appear, or progress, after termination of exposure diminishes its utility in this population. Measurement of urinary chromium at the time of the initial medical surveillance visit is recommended to help identify individuals with high body burdens of chromium, but this measurement is not useful in estimating the risk of an adverse health outcome.

Surveillance for these non-cancer endpoints can be terminated for workers whose initial evaluation is negative. Those with positive findings should undergo follow-up surveillance on an annual basis.

G. Respiratory and Dermal Effects (Formaldehyde)

Occupational exposure to formaldehyde at levels as low as 0.4 ppm has been associated with obstructive patterns on spirometry (Appendix A). These pulmonary function decrements appear to be reversible upon cessation of exposure. Dermal and aerosol contact with formaldehyde has been associated with allergic contact dermatitis and eczema. The levels associated with skin reactions have not been systematically quantified, but as with other contact allergens, some individuals may be expected to react at very low levels, and to have persistent sensitivity once removal from exposure has occurred.

Surveillance for asthma can be accomplished through a respiratory questionnaire, physical examination, and spirometry with and without bronchodilator. If spirometry is negative in the face of a positive history, methacholine challenge testing may improve the sensitivity of the surveillance regimen, but its utility in a surveillance program is hindered by its high cost. Surveillance for symptomatic contact dermatitis, possibly due to formaldehyde, can be easily accomplished through a history and physical examination. Recommendations may be then be offered for specific dermatologic testing, and secondary prevention may be accomplished through avoidance of further exposure, and pharmacologic therapy.

Surveillance for these non-cancer endpoints can be terminated for workers whose initial evaluation is negative. Those with positive findings should undergo follow-up surveillance on an annual basis.

H. Hypertension and Renal Function (Lead)

Occupational exposure to lead in adults resulting in blood lead concentrations in

the range of 30 to 50 Fg/dL and higher have been associated with discernible, albeit usually subclinical, decrements in performance on neurobehavioral tests. Lower blood lead concentrations, in the range of 5 to 25 Fg/dL, have been associated with increased blood pressure, although the proportion of the variance in blood pressure attributable to lead in these studies is generally low ($r^2 < 0.15$). Recent studies in nonoccupational cohorts have found an association between low blood lead concentrations (5 to 15 Fg/dL) and decrements in renal function assessed by serum creatinine or creatinine clearance. However, a causal relationship is uncertain (i.e., decreased renal function may result in higher blood lead concentrations, rather than the converse).

Most of the studies examining the effects of low level lead exposure have used blood lead concentration, rather than airborne lead exposure, as an independent (or predictor) variable. Although blood lead concentrations were not routinely monitored in the Rocky Flats workforce, it is possible to estimate what blood lead concentrations may have existed based upon likely airborne exposures. The quantitative relationship between airborne lead exposure and blood lead concentration is dependent on numerous factors, including the particle size distribution of the lead aerosol, the magnitude and duration of airborne exposure, and baseline (nonoccupational) lead exposure. In a recent 30 month longitudinal study of the relationship of airborne lead to blood lead among battery workers (mean age 41.8 years, mean seniority 12.8 years) whose airborne lead exposure was usually less than 30 Fg/m^3, the covariate-adjusted coefficient of mean air lead (Fg/m^3) in models of blood lead (Fg/dL) was 1.14 (Hodgkins et al, 1992). In other occupational studies, where the level of airborne exposure was usually much higher, coefficients in the range of 0.03 to 0.5 have been found (Hodgkins et al, 1992). In environmental and experimental studies examining air levels in the range of 9 to 36 Fg/m^3, the mean coefficient is approximately 0.5 (US EPA, 1986). However, these latter studies have considered airborne exposure to occur 24 hours per day, 7 days a week . To convert the relationship to a 40 hour work week, it is necessary to increase the coefficient by a factor of 4.2 (168 hours divided by 40 hours).

If the findings of Hodgkin's et al (1992) are applied to 8 hour, time weighted average lead exposures at Rocky Flats of approximately 10 Fg/m^3, it may be estimated that blood lead concentrations in the mid-20's were encountered. This assessment considers that baseline blood lead concentrations (due to nonoccupational exposure) in the 1950s through mid 1980's were probably in the range of 10 to 20 Fg/dL (Harlan, 1988). Based on the studies outlined in Appendix A, this level of lead exposure may have been associated with an impact on blood pressure and renal function. It is therefore reasonable to include measurement of blood lead concentration, blood pressure, and serum creatinine in the medical surveillance regimen for former lead exposed workers. Former workers whose blood lead concentration at the time of initial medical surveillance is # 5 Fg/dL are unlikely to have accumulated an elevated body burden of lead, and/or are unlikely to manifest an adverse effect of lead on their health. Further surveillance for lead-related health end points should not be continued in these subjects. However for former workers whose current blood lead concentration remains > 5 Fg/dL, lead-related surveillance evaluations should be repeated on an annual basis.

I. Respiratory and Dermal Effects (Nickel)

Although the attack rate is not known, former workers exposed to low concentrations of aerosolized nickel (25 Fg/m^3 or possibly lower) are at risk for developing asthma (Appendix A). Dermal contact with nickel in dusts or fluids is associated with a risk of allergic contact dermatitis, even at low levels of exposure that are not readily quantified. Once nickel sensitivity develops, it may be long lasting, possibly because of ongoing exposure to the widespread presence of nickel products in the general environment.

Surveillance for nickel-related asthma can be accomplished through a respiratory questionnaire, physical examination, and spirometry with and without bronchodilator. If spirometry is negative in the face of a positive history, methacholine challenge testing may improve the sensitivity of the surveillance regimen, but its utility in a surveillance program is hindered by its high cost. Surveillance for symptomatic contact dermatitis, possibly due to nickel, can be easily accomplished through a history and physical examination. Recommendations may be then be offered for specific dermatologic testing (such as nickel salt patch testing), and secondary prevention may be accomplished through avoidance of further exposure, and pharmacologic therapy.

Surveillance for these non-cancer endpoints can be terminated for workers whose initial evaluation is negative. Those with positive findings should undergo follow-up surveillance on an annual basis.

IV. Summary and Discussion

In Section II, we described the roster and database we have created for former Rocky Flats workers and described the way we identified and quantified the exposures to the specific hazards. We also described databases we are developing to record hazardous exposures and demonstrated the development and application of quantitative and risk-based eligibility criteria that would be appropriate for selecting former workers for medical monitoring. The criteria we presented are based on methods currently used to select workers in U.S. industries for medical monitoring. We then applied these criteria to our databases for radiation exposure and the preliminary JEM to determine the number of workers that would be eligible if these criteria were applied. Our results are summarized in Table 11. It is clear from these data that there are former RFETS workers who would benefit from a notification and evaluation program.

We have also demonstrated that we can define the size of the target population, not only for the eligibility criteria we selected, but for any set of criteria deemed appropriate. Moreover, the extensive databases we have constructed and are in the process of completing within the next few months will allow us to quantitatively assess cumulative exposure and to develop and apply risk-based criteria if these are deemed appropriate. Furthermore, because we have data for chemical and radiation exposures for individual former workers, we can identify those who were exposed to multiple agents and consider this in our selection of eligibility criteria.

In Section III, we described the types of health impacts that are anticipated for

the levels of exposure used in the eligibility criteria. We also presented and evaluated diagnostic tests that could be employed in a medical monitoring program and made recommendations regarding the ones we think are appropriate for former RFETS workers. Although we did not demonstrate it in this report, we can easily estimate the total number of workers eligible for each component of the medical monitoring program, taking into account exposures to multiple agents, and the fact that many of the exposures to different agents would lead to eligibility to the same screening tests. The outcome will be a customized screening schedule for each worker that takes into account multiple risks and eligibility criteria.

The purpose of this report is to document the need for medical monitoring based on objective criteria and to show that we can identify eligible workers and offer them medical evaluations that would be of benefit to them. We also can identify former workers who do not have complete exposure histories and make estimates of past exposures based on data from other workers with similar jobs. Perhaps a more difficult task is the final selection of eligibility criteria so that risks from chemical and radiation exposure are treated in a similar manner, and that the population of former workers agrees with and supports the criteria. Although we have not achieved this goal, we are maintaining a continuing dialog with representatives of former workers and have compiled the data necessary to make an informed decision.

Table 1. Descriptive Data for Former Rocky Flats Workers

	All Former Workers (N=19,218)	**Former Production Workers** (N=14,429*)	**Former Cleanup Workers** (N=4,723*)
Gender	Number (%)	Number (%)	Number (%)
Males	14,690 (76.5)	11,332 (78.7)	3,311 (70.1)
Females	4,505 (23.5)	3,076 (21.3)	1,410 (29.9)
Unknown	23 (0.1)		
Race	Number (%)	Number (%)	Number (%)
White	14,165 (85.9)	11,227 (85.9)	2,932 (86.1)
Black	605 (3.7)	491 (3.8)	114 (3.3)
Oriental	272 (1.6)	164 (1.3)	106 (3.1)
American Indian	77 (0.5)	49 (0.4)	28 (0.8)
Hispanic	1346 (8.2)	1,128 (8.6)	217 (6.4)
Other	24 (0.1)	16 (0.1)	8 (0.2)
Unknown	2,729 (14.2)	1,354 (9.4)	1,318 (27.9)
Vital status			
Alive	14,957 (78.7)	11,077 (77.5)	3,817 (81.9)
Unknown	4,058 (21.3)	3,212 (22.5)	845 (18.1)
	Mean (SD)	Mean (SD)	Mean (SD)
Age (yr)	51.5 (13.1)	54.3 (12.6)	42.7 (10.5)
Years employed	8.2 (8.5)	10.0 (9.0)	2.7 (1.7)

*Production status is not known for 66 former workers

Table 2. Distribution of Cumulative Doses for All Former Workers

Dose Range (rem)	Gamma Dose	Neutron Dose	Total Penetrating
0-9	12,807 (99.9)	12,792 (99.8)	12,245 (95.5)
10-19	15 (0.1)	14 (0.1)	378 (2.9)
20-29	0	7 (0.1)	90 (0.7)
30-39	0	4 (<0.1)	52 (0.4)
40-49	0	2 (<0.1)	29 (0.2)
50-59	0	1 (<0.1)	14 (0.1)
60-129	0	2 (<0.1)	14 (0.1)
Total	12,822	12,822	12,822

Note: all doses 10 rem and above were received by production workers only

Table 3. Distribution of Estimates of Systemic Burden for Former Production Workers

Percent	Plutonium 239/241	Americium 239/241
0	2,415 (27.3)	5,391 (61.0)
0-4	5,644 (63.9)	3,279 (37.1)
5-9	476 (5.4)	131 (1.5)
10-49	277 (3.1)	29 (0.3)
50-99	12 (0.1)	0 (<0.1)
>=100	7 (0.1)	1 (<0.1)
Total	8,832	8,831

Note: These data do not include contractors or consultants

Table 4. Detection of Specific Radionuclides in Lung Counts for Former Workers

Radionuclide	Not Detected	Detected	Not Analyzed
Plutonium-239	8,280 (43.0)	471* (2.4)	10,467 (54.4)
Americium-241	8,277 (43.0)	474* (2.5)	10,467 (54.4)
Uranium-238	3,379 (17.6)	19 (0.1)	15,820 (82.3)
Thorium-234	1,209 (6.3)	1 (<0.1)	18,008 (93.7)

*470 former workers with positive Pu-239 have positive Am-241; 4 have positive Am-241 with negative Pu-239; one with positive U-238 has positive Pu-239 and Am-241; one with positive Th-238 has positive U-238.

Table 5. Chemical Exposures to Rocky Flats Production Workers

Chemical	Maximum Concentration	ACGIH TLV	Maximum Exposure Period (hours)	Cumulative Annual Exposure (236 days/yr)
Asbestos	40 fiber/cc	2 fiber/cc	0.8	18,880 fiber-hr/cc (lifetime)
Beryllium	4.66 ug/m^3	2.0 ug/m^3	8	8,798 ug-hr/m^3-yr
Carbon tetrachloride	100 ppm	5.0 ppm	8	23,600 ppm-hr/yr
Chromium	160 ug/m^3	50 ug/m^3	3.2	120,832 ug-hr/m^3-yr
Formaldehyde	7 ppm	0.3 ppm	0.8	1,321 ppm-hr/yr
Lead	100 ug/m^3	50ug/m^3	0.8	18,880 ug-hr/m^3-yr
Methylene chloride	250 ppm	50 ppm	2.0	118,000 ppm-hr/yr
Nickel	200 ug/m^3	1,000 ug/m3 (insol.) 100 ug/m^3 (sol.)	3.2	151,040 ug-hr/m^3-yr
Perchloroethylene	250 ppm	25 ppm	4	236,000 ppm-hr/yr
Trichloroethane/ Trichloroethylene	250 ppm	10 ppm/50 ppm	4	236,000 ppm-hr/yr

Table 6. OSHA Precedents for Medical Surveillance Eligibility and Corresponding Medical Monitoring Eligibility Criteria

Exposure	OSHA Standard Number (Year)	PEL (TWA-8)	AL (TWA-8)	OSHA Medical Surveillance Triggers	Corresponding Former Worker Medical Surveillance Triggers
Asbestos	1910.1001 (1996)	0.1 fiber/cc	None	Exposure above the PEL or EL (1 fiber/cc)	PEL: (0.1 fiber/cc) x (8 hr) = 0.8 fiber-hr/cc-yr EL: (1 fiber/cc) x (0.5 hr) = 0.5 fiber-hr/cc-yr
Formaldehyde	1910.1048 (1987)	1 ppm	0.5 ppm	Exposure at or above the AL or exceeding the STEL (2 ppm TWA-15 minutes) Signs or symptoms of toxicity	AL: (0.5 ppm) x (8 hr) = 4 ppm-hr/yr STEL: (2 ppm) x (0.25 hr) = 0.5 ppm-hr/yr Historical reports of symptoms
Lead	1910.1025 (1978)	50 ug/m^3	30 ug/m^3	Exposure above the AL for more than 30 d/year	AL: (30 ug/m^3) x (30 d) x (8 hr/day) = 7,200 ug-hr/m^3-yr
Methylene Chloride	1910.1052 (1997)	25 ppm	12.5 ppm	Exposure at or above the AL for 30 days or more in any year, or above the PEL or STEL (125 ppm TWA-15 minutes) for any time period Emergency exposure, regardless of airborne concentrations Identified by a physician or other licensed health care professional as being at risk for cardiac disease or other serious MC-related health condition All who request inclusion in the medical surveillance program	AL: (12.5 ppm) x (30 d) x (8 hr/d) = 3,000 ppm-hr/yr at or above the AL PEL: (25 ppm) x (1 d) x (8 hr/d) = 200 ppm-hr/yr at or above the PEL STEL: (125 ppm) (1 d) x (0.25 hr/d) = 31.25 ppm-hr/yr at or above the STEL History of unmeasured emergency or accidental releases

PEL = OSHA permissible exposure level; AL = action level; EL = exposure; see text for explanation

Table 7. Eligibility Criteria for Cancer and Other Chronic Diseases Based on Occupational Exposure Limits

Exposure	OSHA PEL (Proposed Update)	ACGIH TLV (Proposed Update)	NIOSH REL*	Proposed Eligibility Criteria**
Beryllium	2 ug/m^3	2 ug/m^3	0.5 ug/m^3	(0.5) x (0.5 ug/m^3) x (30 d) x (8 hr/d) = 60 ug-hr/m^3-yr
Carbon Tetrachloride	10 ppm (2 ppm)	5 ppm	2 ppm 1-hour TWA	(0.5) x (2 ppm) x (30 d) x (1 hour/day)=30 ppm-hr/yr
Chromium (hexavalent), as chromates	100 ug/m^3 (full standard in rule-making)	50 ug/m^3	1 ug/m^3	(0.5) x (1 ug/m^3) x (30 d) x (8 hr/d) = 120 ug-hr/m^3-yr

Nickel metal and other compounds	1,000 ug/m^3 (metal) 100 ug/m^3 (soluble compounds)	1,000 ug/m^3 (metal/insoluble) 100 ug/m^3 (soluble compounds)	15 ug/m^3	(0.5) x (15 ug/m^3 x (30 d) x (8 hr/d) = 1,800 ug-hr/m^3-yr
Tetrachloroethylene (Perchloroethylene)	100 ppm (25 ppm)	25 ppm	Lowest feasible concentration	(0.5) x (25 ppm) x (30 d) x (8 hr/d) = 3,000 ppm-hr/yr
1,1,2-Trichloroethane	10 ppm	10 ppm	10 ppm	(0.5) x (10 ppm) x (30 d) x (8 hr/d) = 1,200 ppm-hr/yr
Trichloroethylene	100 ppm (50 ppm)	50 ppm	Lowest feasible concentration	(0.5) x (50 ppm) x (30 d) x (8 hr/d) = 6,000 ppm-hr/yr

*NIOSH has designated each of these agents a human carcinogen

**Based on exposure at or above 50% of lowest of the three (OSHA, ACGIH, and NIOSH) numeric exposure criteria for 30 or more days per year

Table 8. Eligibility Criteria and Estimates of Eligible Workers Based on Risk for Cancer and Other Chronic Diseases

Exposure	Eligibility Criteria Based on OSHA Policy Precedent	Number of Eligible Workers Based on Average Exposure Estimates	Number of Eligible Workers Based on Highest Exposure Estimates
Asbestos	0.5 fiber-hr/cc-yr	1,089	1,089
Beryllium	60 ug-hr/m^3-yr	972	972
Carbon Tetrachloride	30 ppm-hr/yr	985	985
Chromium (hexavalent), as chromates	120 ug-hr/m^3-yr	1,127	1,127
Methylene Chloride	31 ppm-hr/yr	145	145
Other Chlorinated Solvents: Tetrachloroethylene (Perc) 1,1,2 trichloroethane (TCA) Trichloroethylene (TCE)	1200 ppm-hr/yr	2,914	2,914
Formaldehyde	0.5 ppm-hr/yr	82	82
Lead	7,200 ug-hr/m^3-yr	457	625
Nickel metal and other compounds	1,800 ug-hr/m^3-yr	1,117	1,127

Table 9. Eligibility Criteria and Estimates of Eligible Workers for Non-Cancer Chronic Health Endpoints Based on LOAELs

Exposure	LOAEL-Based Eligibility Criteria (Disease)	Number of Eligible Workers Based on Average Exposure Estimates	Number of Eligible Workers Based on Highest Exposure Estimates
Asbestos	10 fiber-yr/cc lifetime cumulative dose (10 fiber-yr/cc) x (1,888 hr/yr) = 18,880 fiber-hr/cc lifetime cumulative dose (asbestosis)	184	354
Beryllium	0.01 ug/m^3 x 1,888 hr/yr = 18.88 ug-hr/m^3-yr (chronic beryllium disease)	972	972
Carbon Tetrachloride	18,880 ppm-hr/yr (serum bilirubin elevation, liver damage)	322	369
Chromium (hexavalent), as chromates	2 ug/m^3 chromic acid mist x 1,888 hr/yr = 3,776 ug-hr/m^3-yr (asthma)	758	1,038
Methylene Chloride	16 ppm x 1,888 hr/yr = 30,208 ppm-hr/yr (neurobehavioral effects)	145	145
Other Chlorinated Solvents: Tetrachloroethylene (Perc) 1,1,2 trichloroethane (TCA) Trichloroethylene (TCE)	16 ppm x 1,888 hr/yr = 30,208 ppm-hr/yr (steatosis, liver damage)	15	1,685
Formaldehyde	1 ppm x 1,888 hr/yr = 1,888 ppm-hr/yr (asthma)	0	0
Lead	25 ug/m^3 x 1,888 hr/yr = 47,200 ug-hr/m^3-yr (hypertension, renal damage)	0	0

Nickel metal and other compounds	4.2-25.5 ug/m^3 soluble compound 12.5 ug/m^3 x 1,888 hr/yr = 23,600 ug-hr/m^3-yr (asthma)	513	790

*Developed from human lowest observed adverse effect levels (LOAELS) from published literature

Table 10. Components of Medical Monitoring Programs for Cancer

Exam Component	Rocky Flats MMFRW	Fernald General Public	Oregon State Penitentiary
History			
Medical history and review of systems	x	x	x
Occupational exposure history	x		
Environmental exposure history	x	x	
Family medical history		x	
Physical Examination			
Routine physical exam	x	x	

Targeted physical exam			x
Digital prostate	x	x	x
Pelvic exam		x	
Additional tests			
Clinic			
Electrocardiogram (EKG)	x	x	
Pulmonary function test	x	x	
Audiogram	x		

Chest X-ray	x	x	
Vision testing	x		
Testicular ultrasonography			x
Laboratory			
Complete blood count		x	
Chemistry profile		x	
Routine urinalysis		x	
Fecal occult blood	x	x (>40 years of age)	

Prostate-specific antigen	**x (if requested)**		
Pap smear		**x**	
Banked serum, urine & peripheral blood		**x**	
Cytogenetic studies	**planned**	**x**	
Health risk appraisal			
Cancer risk appraisal		**x**	
Exam frequency	**3 years**	**Variable***	**1 year**

*Annual screening for high risk persons; others get annual health questionnaire and review of systems

Table 11. Summary of Medical Monitoring Eligibility for Different Exposures

Agent	Health End Point	Range of Eligible Workers	Reference Table
Ionizing Radiation (Total Penetrating Dose)	Cancer	199 - 577	2
Ionizing Radiation (Systemic Burden)	Cancer	296 - 772*	3
Ionizing Radiation (Lung Counting)	Cancer, pulmonary Fibrosis	271 - ???*	4
Asbestos	Cancer	1089	8
	Asbestosis	1053	9
Beryllium	Cancer & berylliosis	972 (high-risk workers)	8,9
Carbon Tetrachloride	Cancer, liver disease, and neurobehavioral effects	985	
	Liver disease and neurobehavioral effects	322 - 369	
Chromium (hexavalent) as chromates	Cancer	1,127	8
	Respiratory, dermal, and renal damage	758 - 1,038	9
Methylene chloride	Cancer	145	8
Other chlorinated solvents	Cancer	2,914	8
	Liver disease and neurobehavioral effects	15 - 1,685	9
Formaldehyde	Cancer	82	8
	Respiratory & dermal effects	0	9
Lead	Hypertension & renal function	0 - 625	8,9
Nickel metal & other compounds	Cancer	1,117 - 1,127	8
	Respiratory & dermal effects	513 - 790	9

*Upper estimate is uncertain due to high percentage of workers with no analysis results

Appendix A

Review of Non-cancer Health Effects, LOAELs, and Screening Modalities For Specific Chemical Exposures

Review of Non-cancer Health Effects, LOAELs, and Screening Modalities for Specific Chemical Exposures

In this appendix, systematic reviews are presented of non-cancer chronic health effects, the lowest observed levels or Lowest Observed Adverse Health Effect Levels (LOAELs) at which such effects have been seen in occupational studies, and possible biological monitoring and medical surveillance for each health effect in former workers. These are presented for each chemical with the exception of beryllium, which is reviewed in the main body of the report. The LOAELs from these reviews were used as the bases of the criteria presented in Table 9 for eligibility for screening former workers for non-cancer health effects. In the reviews of screening test, each test was assigned a tier rating, with a value of 1 representing widely available screening tests and 2 representing more specialized and less widely available tests. For comparison, section C lists OSHA-mandated and NIOSH recommended medical surveillance tests. The OSHA/NIOSH tests listed, however, may address both cancer as well as non-cancer health endpoints. Our screening recommendations for each chemical are included in the main body of the report. These reviews and recommendations are preliminary and will be finalized in the first year of Phase II.

Chemical/Hazard: Asbestos

A. Potential analytes for biological monitoring in former workers
None

B. Critical Noncancer Health Effects - Chronic exposure

B.1.0. Asbestosis (pneumoconiosis)

B.1.1. Strength of association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of Exposure*	Citation
Asbestosis mortality	10 fiber-yr/cc[H]	Armstrong et al, 1988
Asbestosis	2 - 5 fiber-yr/cc[HH]	Sluis-Cremer, 1991

*cumulative occupational exposure
[H] crocidolite asbestos; [HH] amphibole asbestos

B.1.3. Evidence for reversibility/persistence of effect in former workers
a. Morbidity/mortality from asbestosis typically appears with a latency of 20 or more years after first exposure, and often appears or progresses during retirement

B.1.4. Susceptible populations or special risk factors that increase risk of asbestosis
a. Asbestosis risk possibly increased in smokers (Welch et al, 1994)

B.1.5. Potential tests for medical surveillance in former workers - asbestosis

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/ Questionnaire	1	Moderate	Low	Low	Supportive medical care (e.g. early use of supplemental O_2)
Chest exam	1	Low to moderate	Moderate	Low	Same
Chest x-ray	1	Moderate to high	Moderate to high	Moderate	Same
Spirometry	1	Low to moderate	Low	Moderate	Same

C. OSHA/NIOSH Medical Surveillance Tests
a. Chest X-ray, spirometry

Chemical/Hazard: Carbon Tetrachloride

A. Potential analytes for biological monitoring in former workers
None. Parent compound and metabolites excreted within hours to weeks (Paustenbach et al, 1988).

B. Critical Health Effects - Chronic exposure

B.1.0. Hepatocellular degeneration and necrosis, possibly followed by cirrhosis

B.1.1. Strength of association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of exposure	Citation
Serum transaminases and bilirubin (mild elevation)	210 ppm (avg)	Barnes & Jones (1967)
Serum bilirubin (icteric index)	12 - 60 ppm	Smyth et al (1936)
Cirrhosis	Not stated	McDermott & Hardy (1963)

B.1.3. Evidence for reversibility/persistence of effect in former workers
a. No existing studies of hepatic function in retirees
b. CCl_4 related hepatic fibrogenesis may decrease 6 weeks after exposure is terminated in rats (Belyaev et al, 1992)

B.1.4. Susceptible populations or special risk factors that increase hepatic effects of CCl_4
a. Chronic or repeated ingestion of ethanol (rats) (Hall et al, 1990)
b. Exposure to isopropyl alcohol (humans) (Folland, 1976)
c. PCBs, PBBs, phenobarbital and other inducers of broad spectrum mixed function oxidases
d. Trichloroethylene exposure (Pessayre et al, 1982)

B.1.5. Potential tests for medical surveillance in former workers - hepatic effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Serum transaminases (ALT, AST, GGT) Serum bilirubin	1	Moderate	Low	Low	Avoidance of other hepatotoxins; Modification of drug regimens
Hepatic ultrasound (Brodkin et al, 1995)	2	Moderate to high?	Unknown	High	Same

B.2.0. Neurobehavioral symptoms and deficits

B.2.1. Strength of Association: known

B.2.2. Specific studies - Human

Endpoint	Level of exposure	Citation
Mild narcosis, fatigue	33 - 124 ppm (mean 80)	Heimann & Ford (1941)
Mild narcosis, nausea	20 - 100 ppm	Elkins (1942)
Nausea, depressive symptoms	45 - 100 ppm	Kazantzis & Bomford (1960)

B.2.3. Evidence for reversibility/persistence of effect in retired workers

a. No existing studies in retired workers exposed predominantly to CCl_4
b. Subjective complaints in CCl_4 workers resolved following improvement in industrial hygiene (Kazantzis & Bomford, 1960)
c. Patients with symptoms alone following nonspecific solvent generally improve following cessation of exposure, but patients with symptomatology plus demonstrable impairment may have persistent deficits (Baker, 1994)

B.2.4. Susceptible populations or special risk factors that increase neurobehavioral effects

a. None determined

B.2.5. Potential tests for medical surveillance in former workers - neurobehavioral effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Questionnaire relating to neuropsychological symptoms (Hogstedt et al, 1984; Spurgeon, 1996)	1	High	Low	Low	Referral for detailed evaluation, possibly followed by: Avoidance of other neurotoxins and psychotropic medication (e.g. antidepressants)

C. OSHA/NIOSH Medical Surveillance

a. Liver function tests, urinalysis

Chemical/Hazard: Chlorinated Solvents: 1,1,2 Trichloroethylene (TCE)
1,1,2 Trichloroethane (TCA)
Perchlorethylene (PCE)
Methylene Chloride ($MeCl_2$)

A. Potential analytes for biological monitoring in former workers
None. Parent compounds and metabolites excreted within hours to weeks (Sato et al, 1977; Fernandez et al, 1976; DiVincenzo et al, 1981)

B. Critical Noncancer Health Effects - Chronic Exposure

B.1.0. Steatosis, hepatocellular degeneration and necrosis, possibly followed by cirrhosis (PCE)

B.1.1. Strength of association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of exposure	Citation
Sulfobromophthalein retention; increased urinary urobilinogen	232 - 385 ppm	Coler & Rossmiller, 1953
Hepatic parenchymal change assessed by ultrasound, consistent with steatosis	16 ppm (avg)	Brodkin et al, 1995

B.1.3. Evidence for reversibility/persistence of hepatic effects in former workers
a. Unknown. No existing studies of hepatic function in former workers

B.1.4. Susceptible populations or special risk factors that increase hepatic effects of PCE
a. None determined

B.1.5. Potential tests for medical surveillance in former workers - hepatic effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Serum transaminases (ALT, AST, GGT) Serum bilirubin	1	Moderate	Low	Low	Avoidance of other hepatotoxins; Modification of drug regimens
Hepatic ultrasound (Brodkin et al, 1995)	2	Moderate to high	Unknown	High	Same

B.2.0. Neurobehavioral symptoms and deficits (TCE, PCE, $MeCl_2$, solvent mixtures)
B.2.1. Strength of association: known

B.2.2. Selected specific studies - Humans

Endpoint	Solvent	Level of Exposure	Citation
Fatigue	TCE	200 ppm (for 5 days)	Stewart et al, 1970
Impaired cognition/mood	TCE	260 - 420 ppm	Rasmussen et al, 1993
Attention; memory (slight effect)	$MeCl_2$	100 -225 ppm (avg)	Lash et al, 1991
Coordination	PCE	100 ppm (11 weeks)	Stewart et al, 1977
Attention; cognitive function	PCE	12 - 53 ppm (avg)	Seeber, 1989
Attention; memory; other neurobehavioral parameters	Mixed solvents	Not specified	Bowler et al, 1991

B.2.3. Evidence for reversibility/persistence of effect in former workers

a. Lash et al (1991) detected subtle effects in retired workers, but differences from referents were not statistically significant.
b. Bowler et al (1991) found effects in former workers with nonquantified exposure to mixed chlorinated solvents in the microelectronics industry
c. Patients with symptoms alone following nonspecific solvent generally improve following cessation of exposure, but patients with symptomatology plus demonstrable impairment may have persistent deficits (Baker, 1994)

B.2.4. Susceptible populations or special risk factors that increase chronic neurobehavioral effects of chlorinated solvents

a. None determined

B.2.5. Potential tests for medical surveillance in former workers - neurobehavioral effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Questionnaire relating to neuropsychological symptoms (Hogstedt et al, 1984; Spurgeon, 1996)	1	High	Low	Low	Referral for detailed evaluation, possibly followed by: Avoidance of other neurotoxins and psychotropic medication (e.g. antidepressants)

C. OSHA/NIOSH Medical Surveillance

c. Liver function tests, urinalysis, spirometry, laboratory surveillance at the discretion of the examining physician (e.g. blood COHb for methylene chloride

Chemical/Hazard: Chromium (VI)

A. Potential analytes for biological monitoring in former workers
Excretion of chromium in the urine of manual metal arc welders of stainless steel appears to follow a three-compartment model in which the terminal component has a half-life of 3 to 5 years. Urinary chromium measurements may thus remain elevated for several years following cessation of exposure in individuals with a history of high exposure (Welinder et al, 1983; Aitio et al, 1988)

B. Critical Health Effects - Chronic exposure

B.1.0. Inflammation or atrophy of nasal mucosa

B.1.1. Strength of association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of Exposure	Citation
Nasal mucosal inflammation or atrophy	0.001 - .002 mg/m^3	Lindberg & Hedenstierna (1983)
Nasal mucosal inflammation	0.007 mg/m^3	Cohen et al, 1974

B.1.3. Evidence for reversibility/persistence of effect in former workers
a. Nasal mucosal inflammation may be reversible upon removal from exposure (Lindberg & Hedenstierna, 1983)

B.1.4. Susceptible populations or special risk factors that increase nasal effects of chromium
a. None determined

B.1.5. Potential tests for medical surveillance in former workers - nasal effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Physical exam	1	High	Moderate	Low	Avoidance of irritant exposures

B.2.0. Occupational asthma; reactive airways

B.2.1. Strength of association: known

B.2.2. Selected specific studies - Human

Endpoint	Level of Exposure	Citation
Obstructive patterns on spirometry	0.002 - 0.020 mg/m3	Lindberg & Hedenstierna, 1983
Occupational asthma	Not stated	Olaguibel & Basomba, 1989
Occupational asthma	Not stated	Novey et al, 1983

B.2.3. Evidence for reversibility/persistence of effect in retired workers

a. Although cross-shifts obstructive changes in spirometry were noted, there was no decrement in pre-shift (baseline) pulmonary function in long-term chromic acid exposed workers compared to unexposed controls (Lindberg & Hedenstierna, 1983)

B.2.4. Susceptible populations or special risk factors that increase respiratory effects of chromium

a. None determined

B.2.5. Potential tests for medical surveillance in former workers - chromium asthma

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/ Questionnaire	1	Moderate	Low to moderate	Low	Avoidance of further exposure; pharmacologic therapy; smoking cessation
Physical examination	1	Low	Moderate to high	Low	Same
Spirometry	1	Moderate	Moderate to high*	Mod.	Same
Methacholine challenge	2	High	High*	High	Same

*Specificity for asthma, not necessarily related to chromium

B.3.0. Allergic contact dermatitis

B.3.1. Strength of association: known

B.3.2. Selected specific studies - Human

Endpoint	Level of Exposure	Citation

Allergic contact dermatitis	Not quantified	Shelley, 1964
Allergic contact dermatitis	Not quantified	Thormann et al, 1979
Allergic contact dermatitis	Not quantified	Fregert, 1975

B.3.3. Evidence for reversibility/persistence of effect in retired workers

a. Allergic contact dermatitis to chromium is notoriously persistent, even when putative occupational exposures have been terminated Fiegert, 1975; Thormann et al, 1979)

B.3.4. Susceptible populations or special risk factors that increase dermal effects of chromium

a. None determined

B.3.5. Potential tests for medical surveillance in former workers - dermatitis

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/ Questionnaire	1	Moderate	Low	Low	Avoidance of further exposure; pharmacologic therapy
Physical examination	1	Moderate	Low	Low	Same

B.4.0. Increased urinary levels of low molecular weight proteins indicative of nephrotoxicity

B.4.1. Strength of association: suspected

B.4.2. Selected specific studies - Human

Endpoint	Level of Exposure	Citation
Urinary excretion of Beta-2-microglobulin	0.006 mg/m^3	Lindberg & Vesterberg, 1983
Urinary excretion of retinol binding protein	0.05 - 1.0 mg/m^3 (CrO_3)	Franchini and Mutti 1988

B.4.3. Evidence for reversibility/persistence of effect in retired workers

a. Japanese workers exposed to Cr (VI) for 1-28 years were given complete series of kidney function tests 3 years after exposure ended. All values were within normal limits (Satoh et al. 1981)

b. Elevations in urinary Beta-2-microglobulin observed in current chromium-exposed workers but not present in former workers compared to controls (Lindberg & Vesterberg,1983)

B.4.4. Susceptible populations or special risk factors that increase renal effects of Cr(VI)

a. None determined

B.4.5. Potential tests for medical surveillance in former workers - renal effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Serum creatinine	1	Low to moderate	Moderate	Low	Avoidance of nephrotoxins; modification of drug regimens and nutrition
Urinary retinol binding protein	2	Moderate	Moderate	Moderate	Same

C. OSHA/NIOSH Medical Surveillance
   a. Chest X-ray, spirometry

Chemical/Hazard: Formaldehyde

A. Potential analytes for biological monitoring in former workers
None. Formaldehyde is rapidly metabolized, and blood levels from exogenous exposures are generally much lower than levels resulting from endogenous metabolic processes (Clary & Sullivan, 1992; Heck et al, 1985)

B. Critical Health Effects - Chronic exposure

B.1.0. Occupational asthma

B.1.1. Strength of Association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of exposure	Citation
Obstructive patterns on spirometry; respiratory symptoms	1.13 ppm (mean)	Malaka & Kodama (1990)
Obstructive patterns on spirometry	0.4 ppm (mean)	Alexandersson & Hedenstierna (1989)
Obstructive patterns on spirometry	0.69 ppm (mean)	Horvath et al, (1988)

B.1.3. Evidence for reversibility of effect in retired workers
a. Respiratory impairments reversed four weeks after termination of exposure in exposed woodworkers (Alexandersson & Hedenstierna 1989)
b. Although cross-shifts obstructive changes in spirometry were noted, there was no decrement in pre-shift (baseline) pulmonary function in long-term formaldehyde-exposed workers compared to unexposed controls (Horvath et al, 1988)

B.1.4. Susceptible populations or special risk factors that increase respiratory effects of formaldehyde
a. Cigarette smoking (Alexandersson & Hedenstierna,1989)
b. Dusty environments, or concurrent exposure to formaldehyde and respirable particles may increase the risk of formaldehyde effects on the lower respiratory tract (Green et al, 1989; Malaka & Kodama, 1990;)

B.1.5. Potential tests for medical surveillance - formaldehyde asthma

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/Questionnaire	1	Moderate	Low to moderate	Low	Avoidance of further exposure; pharmacologic therapy; smoking cessation
Physical examination	1	Low	Moderate to high	Low	Same
Spirometry	1	Moderate	Moderate to high*	Mod.	Same
Methacholine challenge	2	High	High*	High	Same

*Specificity for asthma, not necessarily related to formaldehyde

B.2.0. Allergic contact dermatitis

B.2.1. Strength of association: known

B.2.2. Specific studies - Human

Endpoint	Level of Exposure	Citation
Allergic contact dermatitis	Not stated	Pederson, 1980
Contact urticaria	Not stated	Lindskov, 1982

B.2.3. Evidence for reversibility/persistence of effect in retired workers

a. No existing studies of persistent allergic contact dermatitis in retired workers

B.2.4. Susceptible populations or special risk factors that increase allergic effects of formaldehyde

a. None identified

B.2.5. Potential tests for medical surveillance in former workers - dermatitis

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/ Questionnaire	1	Moderate	Low	Low	Avoidance of further exposure; pharmacologic therapy
Physical examination	1	Moderate	Low	Low	Same

C. OSHA/NIOSH Medical Surveillance

a. Spirometry

Chemical/Hazard: Lead (inorganic)

A. Potential analytes for biological monitoring in former workers

a. Blood lead reflects the amount of lead currently circulating in the soft tissues. In

retired workers, it may be strongly influenced by the larger stores of lead in bone, which have a half-life of years to decades (Christoffersson et al, 1984; Erkkila et al, 1992)

b. Bone lead, which may be measured non-invasively by K x-ray fluorescence, may be a biomarker of long-term, cumulative lead exposure (Christoffersson et al, 1984; Erkkila et al, 1992)
c. In retired lead workers, slow release of lead from skeletal lead burdens may contribute to elevated blood lead concentrations years after lead exposure has ended (Erkkila et al, 1992; O'Flaherty, 1993)

B. Critical Noncancer Health Effects - Chronic exposure

B.1.0. Neurobehavioral deficits (adults)

B.1.1. Strength of association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of exposure*	Citation
Decreased performance on neurobehavioral tests	Blood lead 27 ug/dL (mean TWA)	Mantere et al, 1984
Decreased performance on neurobehavioral tests	Blood lead 52.2 ug/dL (mean; range 45 - 60)	Campara et al, 1984
Decreased performance on neurobehavioral tests	Blood lead 51.8 ug/dL (mean, range 41 -80)	Stollery et al, 1991

*Studies have generally reported blood lead of subjects rather than external measures of exposure. See discussion in section D below.

B.1.3. Evidence for reversibility/persistence of effect in retired workers

a. Although not directly addressed by existing studies, some investigations reveal a stronger association of neurobehavioral performance with recent exposure than with cumulative exposure (Balbus - Kornfeld et al, 1995).

B.1.4. Susceptible populations or special risk factors that may increase the neurobehavioral effects of lead

a. Lead absorption may be increased in the presence of iron deficiency (Watson et al, 1980), or in individuals with a diet low in calcium (Hernandez-Avila et al, 1996).

B.1.5. Potential tests for medical surveillance in former workers--neurobehavioral effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Questionnaire relating to neurobehavioral symptoms (Hogstedt et al, 1984; Spurgeon, 1996)	1	high	low	low	Referral for detailed evaluation, possibly followed by: Avoidance of other neurotoxins and psychotropic medication (e.g. antidepressants)

B.2.0. Hypertension

B.2.1. Strength of association: suspected

B.2.2. Selected specific studies - Human

Endpoint	Level of exposure	Citation
Diastolic blood pressure	Blood lead (2 - 15 ug/dL)	Sharp et al, 1988
Diastolic blood pressure	Blood lead (median 5.6 ug/dL, range 0.5 - 35)	Proctor et al, 1996
Hypertension (defined by BP or medication usage)	Tibia (bone) lead 21.6 ppm (mean) Blood lead 6.3 ug/dL (mean)	Hu et al, 1996

B.2.3. Evidence for reversibility/persistence of effect in retired workers

a. In the Normative Aging Study, a positive association between low levels of blood lead and blood pressure existed in a cohort with a mean age of 66.1 years, (S.D. 7.4 years; range 45 - 93), (Proctor et al, 1996).

B.2.4. Susceptible populations or special risk factors that increase blood pressure effects of lead

a. Black race may be a risk factor for the pressor effects of lead (Sharp et al, 1990)
b. Lead absorption may be increased in the presence of iron deficiency (Watson et al, 1980), or in individuals with a diet low in calcium (Hernandez-Avila et al, 1996)

B.2.5. Potential tests for medical surveillance in former workers - hypertension

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Blood pressure	1	Moderate to high	Moderate to low	low	Lifestyle modification; Antihypertensive medication

History/ Questionnaire (to determine use of antihypertensive medication, or diagnosis of hypertension on other occasions)	1	Moderate to high	Moderate to high	low	Lifestyle modification; Antihypertensive medication

B.3.0. Altered or decreased renal function

B.3.1. Strength of Association (at low level exposure) - suspected

B.3.2. Selected specific studies - Human

Endpoint	Level of exposure*	Citation
Creatinine clearance (decreased)	Blood lead 10 ug/dL (geometric mean; range 1.7 - 72.5)	Staessen et al, 1992
Creatinine clearance (decreased)	Blood lead 8.1 ug/dL (arithmetic mean; range < 5 - 26.0)	Payton et al, 1994
Serum creatinine; longitudinal increase in serum creatinine	Blood lead # 25 ug/dL	Kim et al, 1996

B.3.3. Evidence for reversibility/persistence of effect in retired workers

a. In the Normative Aging Study, an association of blood lead with concurrent serum creatinine, and longitudinal increase in serum creatinine, was found in a cohort of men with median baseline age 56.9 years (range 37.7 - 87.5) (Kim et al, 1996).

B.3.4. Susceptible populations or special risk factors that increase renal effects of lead

a. Lead absorption may be increased in the presence of iron deficiency (Watson et al, 1980), or in individuals with a diet low in calcium (Hernandez-Avila et al, 1996)

B.3.5. Potential tests for medical surveillance in former workers - renal effects

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
Serum creatinine	1	Low to moderate	Moderate	Low	Avoidance of nephrotoxins; Modification of drug regimens and nutrition

Creatinine clearance (24-hour urine collection)	2	Moderate	Moderate	Moderate	Same

C. OSHA/NIOSH Medical Surveillance
   a. Blood lead level, zinc protoporphyrin, hemoglobin, blood urea nitrogen, serum creatinine, urinalysis, complete blood count

Chemical/Hazard: Nickel

A. Potential analytes for biological monitoring in former workers
None. Urine and serum levels of nickel in workers inhaling soluble nickel compounds reflect the amount of nickel absorbed in the previous 1 or 2 days (Templeton [WHO], 1996).

B. Critical Health Effects - Chronic Exposure

B.1.0. Occupational Asthma

B.1.1. Strength of association: known

B.1.2. Selected specific studies - Human

Endpoint	Level of Exposure	Citation
Occupational asthma	4.2 - 25.5 ug/m3	Shirakawa et al, 1990
Occupational asthma	Not stated	Malo et al, 1982
Occupational asthma	Not stated	Block & Young, 1982

B.1.3. Evidence for reversibility/persistence of effect in retired workers

a. Although long-term follow-up studies on former workers exposed to asthma are not available, studies on subjects with occupational asthma from other causes have demonstrated persistence of symptoms and airways hyperresponsiveness after removal of the offending agent (Malo & Cartier, 1996)

B.1.4. Susceptible populations or special risk factors that increase respiratory effects of nickel

a. Potential increased risk with concurrent exposure to chromium (Johansson et al.1989).

B.1.5. Potential tests for medical surveillance in former workers - nickel asthma

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/ Questionnaire	1	Moderate	Low to moderate	Low	Avoidance of further exposure; pharmacologic therapy; smoking cessation
Physical examination	1	Low	Moderate to high	Low	Same
Spirometry	1	Moderate	Moderate to high*	Mod.	Same
Methacholine challenge	2	High	High*	High	Same

*Specificity for asthma, not necessarily related to nickel

B.2.0. Contact dermatitis

B.2.1. Strength of association: known

B.2.2. Specific studies - Human

Endpoint	Level of exposure	Citation
Allergic contact dermatitis	Not stated	Block & Young, 1982
Allergic contact dermatitis	Not stated	Nethercott & Holness, 1990

B.2.3. Evidence for reversibility/persistence of effect in retired workers

a. Sensitivity to nickel as a cause of dermatitis may be persistent (Wubs PL & Spruit, 1979; Keczkes et al, 1982)

B.2.4. Susceptible populations or special risk factors that increase the dermatologic effects of nickel

a. Nickel dermatitis is more prevalent among females, possibly due to increased exposure and sensitization from jewelry (Adams, 1983; Nethercott & Holness, 1990)
b. Blacks may have higher rates of nickel sensitivity in epidemiological studies (ATSDR, 1996b)

B.2.5 Potential tests for medical surveillance in former workers - dermatitis

Test	Tier	Sensitivity	Specificity	Cost	Secondary Prevention
History/ Questionnaire	1	Moderate	Low	Low	Avoidance of further exposure; pharmacologic therapy
Physical examination	1	Moderate	Low	Low	Same

C. OSHA/NIOSH Medical Surveillance
   a. Chest X-ray, spirometry

V. REFERENCES

Adams R.D. (1983). Occupational Skin Disease. Grune & Stratton; San Francisco.

Agency for Toxic Substances and Disease Registry (1996a). Consideration of medical monitoring for Hanford: Draft final document. Atlanta, Georgia.

Agency for Toxic Substances and Disease Registry (1996b), Toxicological Profile for Nickel.

Aitio A., Jarvisalo J., et al. (1988). "Chromium," in Biological Monitoring of Toxic Metals, Clarkson, T., Friberg L., Nordberg G.F., Sager P., eds. Plenum Press; New York, pp. 369-82.

Alexandersson R., Hedenstierna G. (1989). Pulmonary function in wood workers exposed to formaldehyde: a prospective study. Arch Environ Health. 44:5-11.

Armstrong B.K., De Klerk N.H., et al. (1988). Mortality in miners and millers of crocidolite in Western Australia. Brit J Ind Med. 45:5-13.

Baker E.L. (1994). A review of recent research on health effects of human occupational exposure to organic solvents: a critical review. J Occup Med. 36:1079-92.

Balbus-Kornfeld J.M., Stewart W., et al. (1995). Cumulative exposure to inorganic lead and neurobehavioral test performance in adults: an epidemiological review. Occup Environ Med. 52:2-12.

Barnes R., Jones R.C. (1967). Carbon tetrachloride poisoning. Am Ind Hyg Assoc J. 28:557-60.

Belyaev N.D., Budker V.G., et al. (1992). Liver plasma membrane-associated fibroblast growth: stimulatory and inhibitory activities during experimental cirrhosis. Hepatology. 15:525-31.

Block G.T., Yeung M. (1982). Asthma induced by nickel. JAMA. 247:1600-2.

Bobka C.A., Stewart L.A., Engelken G.J., Golitz L.E., Newman L.S. (1997). Comparison of *in vivo* and *in vitro* measures of beryllium sensitization. J Occup Environ Med. (In press).

Bowler R.M., Mergler D., et al. (1991). Neuropsychological impairment among former microelectronics workers. NeuroToxicology. 12:87-104.

Brodkin C.A., Daniell W., et al. (1995). Hepatic ultrasound changes in workers exposed to perchloroethylene. Occup Environ Med. 52:679-85.

Byers T., Donnegan W., Greenwald P., McDonald C., Moss R., and Bailey S. (1997). ACS Blue Ribbon Advisory Group on Community Cancer Control: Report of the Detection Workshop.

Byers T., Levin B., Rothenberger D., Dodd G.D., Smith R.A. (1997). American Cancer Society guidelines for screening and surveillance for early detection of colorectal polyps and cancer: update 1997. CA - A Cancer Journal for Clinicians. 47:154-160

Campara P., D'Andrea F., et al. (1984). Psychological performance of workers with blood-lead concentration below the current threshold limit value. Int Arch Occup Environ Health. 53:233-46.

ChemRisk (1991a). Rocky Flats Historical Investigation Interviews. Repository Document RE-891. January, 1991. Prepared for the Colorado Department of Health.

ChemRisk (1991b). Task 1 Report: Identification of Chemicals and Radionuclides used

at Rocky Flats (Draft). January, 1991. Prepared for the Colorado Department of Health.
ChemRisk (August, 1992). Project Tasks 3 and 4 Final Draft Report: Reconstruction of Historical Rocky Flats Operations and Identification of Release Points. Prepared for the Colorado Department of Health.
Christoffersson J.O., Schutz A., et al. (1984). Lead in finger-bone analyzed in vivo in active and retired lead workers. Am J Ind Med. 6:447-57.
Clary J.J., Sullivan J.B. (1992). "Formaldehyde," in Hazardous Materials Toxicology: Clinical Principles of Environmental Health, Sullivan J.B. and Krieger G.R., eds. Williams & Wilkins; Baltimore,.
Cohen S.R., Davis, D.M., et al. (1974). Clinical manifestations of chromic acid toxicity: nasal lesions in electroplate workers. Cutis. 13:558-68.
Coler H.R., Rossmiller H.R. (1953). Tetrachlorethylene exposure in a small industry. Arch Ind Hyg Occup Med. 8:227-33.
DiVincenzo G.D., Kaplan C.J. (1981). Uptake, metabolism, and elimination of methylene chloride vapor by humans. Toxicol Appl Pharmacol. 59:130-40.
Elkins H.B. (1942). Maximum allowable concentrations: I. Carbon tetrachloride. J Ind Hyg Toxicol. 24:233-5.
Erkkila J., Armstrong R., et al. (1992). In vivo measurements of lead in bone at four anatomical sites: long term occupational and consequent endogenous exposure. Brit J Ind Med. 49:631-44.
Fernandez J., Guberan E., et al. (1976). Experimental human exposures to tetrachloroethylene vapor and elimination in breath after inhalation. Am Ind Hyg Assoc J. 37:143-50.
Folland D.S., Schaffner W., et al. (1976). Carbon tetrachloride toxicity potentiated by isopropyl alcohol: investigation of an industrial outbreak. JAMA. 236:1853-6.
Franchini I., Mutti A. (1988). Selected toxicological aspects of chromium (VI) compounds. Sci Total Environ. 71:379-87.
Franke B., and Gurney K.R. (undated). Estimates of lung burdens for workers at the Feed Materials Production Center, Fernald, Ohio.
Fregert S. (1975). Occupational dermatitis in a 10 year material. Contact Dermatitis. 1:96-107.
Green D.J., Bascom R., et al. (1989). Acute pulmonary response in healthy, nonsmoking adults to inhalation of formaldehyde and carbon. J Toxicol Environ Health. 28:261-75.
Hall P.M., Plummer J.L., et al. (1990). Hepatic fibrosis and cirrhosis after chronic administration of alcohol and "low-dose" carbon tetrachloride vapor in the rat. Hepatology. 13:815-9.
Harlan W.R. (1988). The relationship of blood lead levels to blood pressure in the U.S. population. Environ Health Perspectives. 78:9-13.
Heck H., Casanova-Schmitz M., et al. (1985). Formaldehyde concentrations in the blood of humans and Fischer-344 rats exposed to formaldehyde under controlled conditions. Am Ind Hyg Assoc J. 46:1-3.

Heimann H., Ford C.A. (1941). Low concentration of carbon tetrachloride capable of causing mild narcosis. Ind Bull. 20, July-August.
Hernandez-Avila M., Gonzalez-Cossio T., et al. (1996). Dietary and environmental determinants of blood and bone lead levels in lactating postpartum women living in Mexico City. Environ Health Perspectives. 104:1076-82.
Hodgkins D.G., Robins T.G., et al. (1992). A longitudinal study of the relation of lead in blood to lead in air concentrations among battery workers. Brit J Ind Med. 49:241-8.
Hogstedt C., Andersson K., Hane M. (1984) "A Questionnaire Approach to the Monitoring of Early Disturbances in Central Nervous System Function," in Biological Monitoring and Surveillance of Workers Exposed to Chemicals, Aitio A., Riihimaki V., Vainio H., eds. Hemisphere; Washington, pp. 275-87.
Horvath E.P., Anderson H., et al. (1988). Effects of formaldehyde on the mucous membranes and lungs: a study of an industrial population. JAMA. 259:701-6.
Hu H., Aro A., et al. (1996). The relationship of bone and blood lead to hypertension: the normative aging study. JAMA. 275:1171-6.
Johansson A., Curstedt T., et al. (1989). Lung lesions after experimental combined exposure to nickel and trivalent chromium. Env Res. 50:103-19.
Kazantis G., Bomford R.R. (1960). Dyspepsia due to inhalation of carbon tetrachloride vapour. Lancet. 1960:360-2.
Keczkes K., Basheer A.M., et al. (1982). The persistence of allergic contact sensitivity, a 10-year follow-up in 100 patients. Br J Dermatol. 107:461-5.
Kim R., Rotnitzky A., et al. (1996). A longitudinal study of low-level lead exposure and impairment of renal function. JAMA. 275:1177-81.
Kreiss K., Newman L.S., Mroz M.M., Campbell P.A. (1989). Screening blood test identifies subclinical beryllium disease. J Occup Med. 31:603-608.
Kreiss K., Mroz M.M., Zhen B., Martyny J., Newman L.S. (1993). Epidemiology of beryllium sensitization and disease in nuclear workers. Am Rev Respir Dis. 148:985-991.
Kreiss K,. Wasserman S., Mroz M.M., Newman L.S. (1993). Beryllium disease screening in the ceramics industry: Blood test performance and exposure-disease relations. J Occup Med. 35:267-274.
Kreiss K., Mroz M.M., Newman L.S., Martyny J., Zhen B. (1996). Machining risk of beryllium disease and sensitization with median exposures below 2 mg/m^3. Am J Industr Med. 30:16-25.
Lash A.A., Becker C.E., et al. (1991). Neurotoxic effects of methylene chloride: are they long lasting in humans? Brit J Ind Med. 48:418-26.
Lindberg E., Hedenstierna G. (1983). Chrome plating: symptoms, findings in the upper airways, and effects on lung function. Arch Environ Health. 38:367-74.
Lindberg E., Vesterberg O. (1983). Urinary excretion of proteins in chromeplaters, ex-chromeplaters and referents. Scand J Work Environ Health. 9:505-10.
Lindskov R. (1982). Contact urticaria to formaldehyde. Contact Dermatitis.8:333-4.
Malaka T., Kodama A.M. (1990). Respiratory health of plywood workers occupationally

exposed to formaldehyde. Arch Environ Health. 45:288-94.
Malo J.L., Cartier A. (1996). "Occupational Asthma," in Occupational and Environmental Respiratory Disease, Harber P., Schenker M.B., Balmes J.R., eds. Mosby; Chicago.
Malo J.L., Cartier A., et al. (1982). Occupational asthma caused by nickel sulfate. J Allergy Clin Immunol. 69:55-9.
Mantere P., Hanninen H., et al. (1984). A prospective follow-up study on psychological effects in workers exposed to low levels of lead. Scand J Work Environ Health. 10:43-50.
McDermott W.V., Hardy H.L. (1963). Cirrhosis of the liver following chronic exposure to carbon tetrachloride. J Occup Med. 5:249-51.
Nethercott J.R., Holness D.L. (1990). Cutaneous nickel sensitivity in Toronto, Canada. J Amer Acad Dermatol. 22:756-61.
Newman L.S., Kreiss K., King T.E., Jr., Seay S., Campbell P.A. (1989). Pathologic and immunologic alterations in early stages of beryllium disease: Re-examination of disease definition and natural history. Am Rev Respir Dis. 139:1479-1486.
Newman L.S., Buschman D.L., Newell J.D., Jr., Lynch D.A. (1994). Beryllium disease: Assessment with CT. Radiology. 190:835-840.
Novey H.S., Habib M., et al. (1983). Asthma and IgE antibodies induced by chromium and nickel salts. J Allerg Clin Immunol. 72:407-12.
O'Flaherty E.J. (1993). Physiologically based models for bone-seeking elements: IV. Kinetics of lead disposition in humans. Toxicol Appl Pharmacol. 118:1-13.
Olaguibel J.M., Basomba A. (1989). Occupational asthma induced by chromium salts. Allergologia et Immunopathologia. 17:133-6.
Paustenbach D.J., Clewell H.J., et al. (1988). A physiologically based pharmacokinetic model for inhaled carbon tetrachloride. Toxicol Appl Pharmacol. 96:191-211.
Payton M., Hu H., et al. (1994). Low-level lead exposure and renal function in the normative aging study. Am J Epidemiol. 140:821-9.
Pedersen N.B. (1980). Occupational hand eczema from formaldehyde in price labels. Contact Dermatitis. 6:57-8.
Pessayre D., Cobert B., et al. (1982). Hepatotoxicity of trichloroethylene-carbon tetrachloride mixtures in rats. Gastroenterology. 83:761-72.
Proctor S.P., Rotnitzky A., et al. (1996). The relationship of blood lead and dietary calcium to blood pressure in the normative aging study. Int J Epidemiol. 25:528-36.
Rasmussen K., Jeppesen H.J., et al. (1993). Solvent-induced chronic toxic encephalopathy. Am J Ind Med. 23:779-792.
Sato A., Nakajima T., et al. (1977). A pharmacokinetic model to study the excretion of trichloroethylene and its metabolites after an inhalation exposure. Brit J Ind Med. 34:56-63.
Satoh K., Fukuda Y., et al. (1981). Epidemiological study of workers engaged in the manufacture of chromium compounds. J Occup Med. 23:835-8.
Seeber A. (1989). Neurobehavioral toxicity of long-term exposure to tetrachloroethylene. Neurotoxicol Teratol. 11:579-83.

Sharp D.S., Osterloh J., et al. (1988). Blood pressure and blood lead concentration in bus drivers. Environ Health Perspectives. 78:131-7.
Sharp D.S., Benowitz N.L., et al. (1990). Influence of race, tobacco use, and caffeine use on the relation between blood pressure and blood lead concentration. Am J Epidemiol. 131:845-54.
Shelley, W.B. (1964). Chromium in welding fumes as cuase of eczematous hand eruption. JAMA. 189:170-171.
Shirakawa T., Kusaka Y., et al. (1990). Hard metal asthma: cross immunological and respiratory reactivity between cobalt and nickel? Thorax. 45:267-71.
Sluis-Cremer G.K. (1991). Asbestos disease at low exposure after long residence time in amphibole miners. Toxicol Ind Health. 7:89-95.
Smyth H.F., Smyth H.F, Jr., et al. (1936). The chronic toxicity of carbon tetrachloride; animal exposures and field studies. J Ind Hyg Toxicol. 18:277-98.
Spurgeon A. (1996). Current approaches to neurobehavioural testing in occupational health. Occup Environ Med. 53:361-6.
Staessen J.A., Lauwerys R.R., et al. (1992). Impairment of renal function with increasing blood lead concentration in the general population. N Eng J Med. 327:151-6.
Stewart R.D., Dodd H.C., et al. (1970). Experimental human exposure to trichloroethylene. Arch Environ Health. 20:64-71.
Stewart R.D., Hake C.L., et al. (1977). Effects of Perchloroethylene/Drug Interaction on Behavior and Neurological Function., Addendum by V.R. Putz, Medical College of Wisconsin and National Institute of Occupational Safety and Health. Division of Biomedical and Behavioral Science, Cincinnati, OH. Report No. NIOSH-77-191.
Stollery B.T., Broadbent D.E., et al. (1991). Short term prospective study of cognitive functioning in lead workers. Brit J Ind Med. 48:739-49.
Templeton D (1996). "Nickel," in Biological Monitoring of Chemical Exposure in the Workplace, Volume 2. World Health Organization; Geneva.
Thormann J., Jesperson N.B., et al. (1979). Persistence of contact allergy to chromium. Contact Dermatitis. 5:261-4.
United States District Court Southern District of Ohio, Western Division (1994). Class Action Settlement Agreement, Case No. C-1-90-067.
USEPA (1986). Air Quality Criteria for Lead, Volume III of IV (Draft Final). Doc. No. EPA-600/8-83/028cF.
United States Preventive Services Task Force (USPSTF) (1996). Guide to Clinical Preventive Services, Second Edition. Baltimore: Williams & Wilkins, 1996.
University of Cinncinati Medical Center, Barret Cancer Center (1997). Fernald Medical Monitoring Program (proposal).
Watson W.S., Hume R., et al. (1980). Oral absorption of lead and iron. The Lancet. August 2, 236-7.
Welch L.S., Michaels D., et al. (1994). The National Sheet Metal Worker Asbestos Disease Screening Program: radiologic findings. National Sheet Metal Examination Group. Am J Ind Med. 25:635-48.

Welinder H., Littorin M., et al. (1983). Elimination of chromium in urine after stainless steel welding. Scand J Work Env Health. 9:397-403.
Wubs P.L. and Spruit D. (1979). Course of nickel contact dermatitis. Contact Dermatitis. 5:57-8.